The Surgical Treatment of Bladder Cancer

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Chapter 7b:

Prostate-Sparing Cystectomy: Long-Term Oncological Results

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Abstract

Purpose: To analyze the oncological outcome of prostate sparing cystectomy (PSC).

Materials and Methods: Between 1994 and 2006, 63 male patients were treated with Prostate Sparing Cystectomy (PSC) after meeting the inclusion criteria (no tumour at bladder neck, no prostate cancer). Results were compared with patients who underwent standard cystoprostatectomy (SC) during the same study period, after matching for clinical and pathological characteristics.

Results: The 3 and 5-year disease specific survival rates were 77% and 66% in the PSC group and 68% and 64% in the SC group (log-rank, p=0.6). Local recurrence rate was 7.9% and 16% for the PSC and the SC group, respectively. Distant recurrence rate was 29% and 33% for the PSC and SC group, respectively. Subsequent prostate cancer was detected in 3% in the PSC group. None of these patients died of prostate cancer. In the SC group final pathology disclosed 18% prostate cancer.

Conclusions: Local recurrences were not diagnosed more frequently in the PSC group compared to SC. Outcomes of both procedures are comparable with contemporary cystoprostatectomy series. We consider this procedure oncologically safe and offer this to selected patients. However, selection is the key to success and our results should further be corroborated by the experience of others.

Introduction

The standard technique of radical cystectomy in male patients consists of removal of the bladder together with removal of the prostate, seminal vesicles and part of the vasa deferentia. Parasympathetic and sympathetic nerves, essential for a normal sexual response, are often removed or damaged. In order to preserve erectile function, nerve sparing cystoprostatectomy was developed.[1] To improve the success rates, various modified cystectomy techniques followed, with the aim to further improve the preservation of erectile function.[2,3] The techniques and inclusion criteria vary. In some procedures the prostate or part of the prostate remains in situ after transurethral resection of the prostate. While in other procedures the prostate is partially removed with preservation of the vasa deferentia, seminal vesicles and ejaculatory ducts.[4]

In 1994 we started with prostate sparing cystectomy (PSC), (initially named sexuality preserving cystectomy and neobladder, SPCN), in a selected group of patients. Aim was preservation of sexual function with anatomic reconstruction of the lower urinary tract without compromising the oncological results. The indications, technical aspects, functional and oncological results have been published.[5] A cystectomy is performed, after lymph node dissection, with preservation of the prostate, seminal vesicles and vasa deferentia. The bladder neck, prostate and prostatic urethra are sampled extensively before PSC, but no effort is made to remove all prostatic urothelium.

Patients considered for this procedure represent a selection of the population presenting with bladder cancer and the majority of patients are not eligible for a PSC (tumour at the bladder neck and/or prostate cancer) and are treated with a "standard" cystoprostatectomy (SC) with or without an orthotopic bladder substitution. In this study we assessed retrospectively the oncological results of PSC and SC in a cohort of patients treated at the same institute during the same study period.

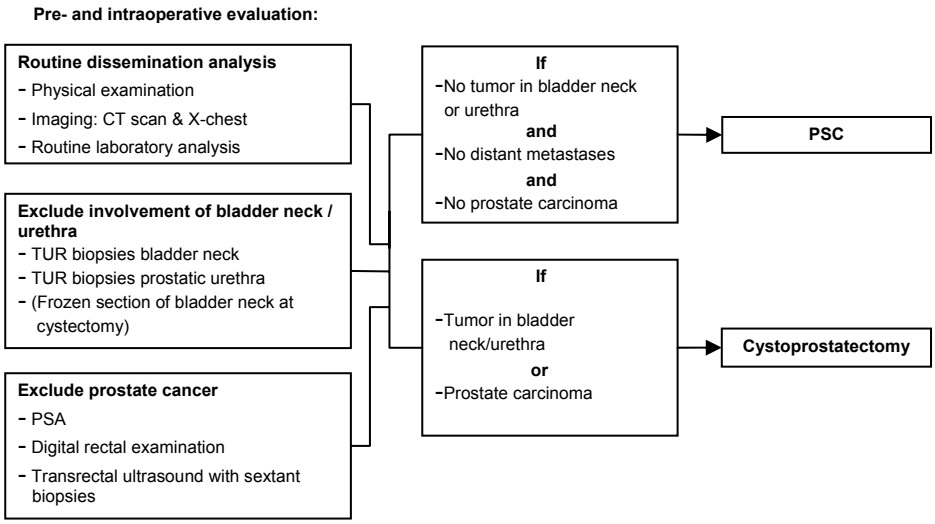
Methods

Between 1994 and 2006, 268 male patients with urothelial cancer were treated with cystectomy and urinary diversion for bladder cancer. 107 males received an ileal conduit, 25 an Indiana pouch, 63 a PSC, and 73 received an orthotopic neobladder.

The inclusion criteria for PSC are; indication for cystectomy and motivation for preserving sexual functions. Exclusion criteria are: tumour localization in the bladder neck or prostatic urethra (excluded by (re)TURB), prostate cancer (excluded by digital rectal examination, Prostate Specific Antigen (PSA), Trans Rectal Ultrasound and biopsies irrespective of PSA levels). In addition, preoperative impotence and patients' decision for a SC were exclusion criteria. The diagnostic work up is summarised in Fig 1. 63 selected male patients were treated with a PSC. After pelvic lymph node dissection, the bladder was removed, leaving the prostate and seminal vesicles in place. Boundaries of pelvic node dissection until 2000 where: distally the circumflex vein and the node of Cloquet, laterally the iliac artery, medially the bladder and the prostate and dorsally the

hypogastric artery and the obturator nerve. From 2000 the boundaries were enlarged proximally to the crossing of the ureter over the common iliac artery, laterally to the genitofemoral nerve and dorsally/caudally the bottom of the obturator fossa. An orthotopic pouch according to Studer is then anastomosed to the outer rim of the prostate in males. Details of the operation technique have been described in previous articles.[5]

Figure 1: *Algorithm of inclusion/exclusion and diagnostic work up*



The SC patients were selected from our cystectomy database and matched for clinicopathological characteristics with the PSC patients from the same database. During the study period 73 male patients were treated with a SC. We excluded patients with urethral tumours, previous radiotherapy with curative intent, and patients with a clinical T4 tumour. 63 patients remained for analysis. Before cystectomy a pelvic lymphadenectomy with the above mentioned boundaries was performed. No attempt was made to preserve the neuro-vascular bundles in all these patients.

All tumours were staged according to the 2002 TNM classification, pathological stage (pT) was assigned to the highest stage after transurethral resection.[6] Tumour positive lymph nodes were considered neither a contra-indication for PSC, nor for standard cystectomy and neo-bladder. These patients were eligible for (neo) adjuvant chemotherapy. Patients were followed every 3 months in the first year, ever 6 months in the next 2 years and then yearly. Oncological follow-up consisted of history, patient self administered question-naires, cystoscopy, urine cytology, CT-imaging, and PSA tests. Pelvic or local recurrences were defined as any urothelial cancer recurrence below the iliac bifurcation within the pelvic soft tissue.

Kaplan-Meier survival estimates were used in survival data analysis and follow up. Log rank tests were performed to compare survival between the two groups. Cox proportional hazards regression analysis was performed to investigate the relation between type of surgery or other factors and disease specific survival. The following variables were included: age, type of surgery (PSC vs SC), tumour extension, margins, and bladder neck infiltration.

Results

Patient characteristics

There were 63 males in the PSC group and 63 males in the SC group. Median age was 55 years in the PSC group and 61 years in the SC group. Median follow-up was 56 months in the PSC group and 76 months in the SC group. In both groups, all patients had a minimal follow up of 12 months, 91% of patients more than two years, and 78% of patients more than three years. Apart from age and follow-up there was no significant difference between the two groups. Patients' characteristics are shown in table 1.

Three patients in the PSC and six patients in the SC group had a grade 2 tumour; all other tumours were poorly differentiated. In the SC group 22 patients had tumour infiltration in the bladder neck. Two patients in the PSC and five patients in the SC group had tumour positive margins after surgery.

Table 1: *Patient characteristics*

All TCC	PSC	SC	p-value
N	63	63	
Median age	55 yr	61 yr	P<0.002
Clinical Tumour stage			
T1,a,is	15	17	
T2	38	31	n.s
T3	10	15	
Clinical N-status			
N0	56	56	n.s
N+	7	7	
Pathological Tumour stage			
T1,0,a,is	16	15	
T2	31	26	n.s
T3	16	19	
T4	-	3	
Pathological N-status			
N0	45	51	
N1	7	4	n.s
N2	11	8	
Bladder Neck infiltration			
yes	-	22	
no	63	41	
Margins			
negative	61	58	n.s
positive	2	5	

Chemotherapy

Eleven patients in the PSC and eight in the SC group received cisplatin based chemotherapy for tumour positive lymph nodes in a neo-adjuvant setting. Adjuvant chemotherapy was given to one patient in the PSC and eight patients in the SC group, all patients had tumour positive lymph nodes. There was no significant difference in chemotherapy setting between the two groups. Six patients in the SC group received palliative chemotherapy at the time of tumour progression.

Oncological outcome

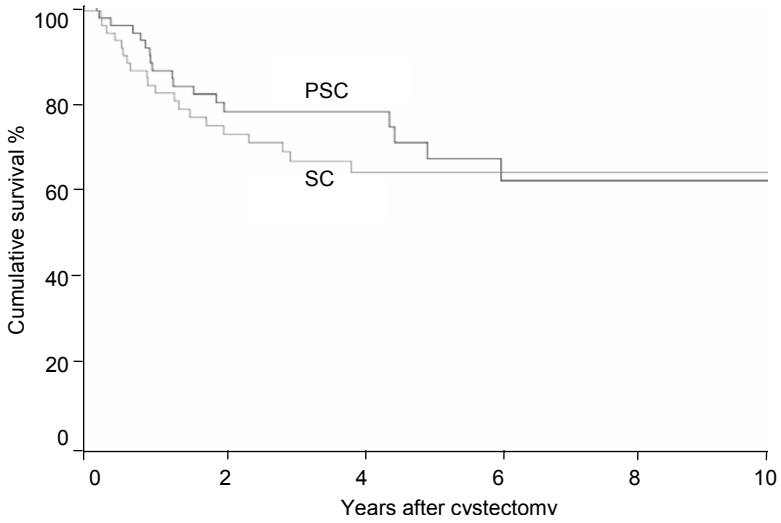
No statistically significant differences were found in local recurrence rate or distant metastases (7.9% and 16%, p=0.1; 29% and 33%, p=0.4 in the PSC and in

the SC, respectively, see table 2). The 3 and 5-year disease specific survival rates were 77% and 66% in the PSC group and 68% and 64% in the SC group (log-rank, p=0.6) (Fig.2).

Table 2: *Local and distant recurrences comparing PSC and SC*

	Recurrence after PSC				Recurrence after SC			
Stage	**local**		**distant**		**local**		**distant**	
pTis,1,2-N0	3/35	9%	7/35	20%	5/34	14%	4/34	12%
pT3-4N0	0/10	0%	4/10	40%	1/17	75%	8/17	47%
pTN+	2/18	11%	7/18	39%	4/12	33%	9/12	75%
Total	5/63	8%	18/63	29%	10/63	16%	21/63	33%

Figure 2: *Disease specific survival of PSC and SC*



In the multivariate analysis, only extravesical disease (HR 3.58, p=0.003) and tumour positive lymph nodes (HR 5.75, p=0.0004) were significantly associated with survival.

Two patients in the PSC group developed prostate cancer, one died after 126 months due to metastatic bladder cancer; the other is still alive at 50 months of follow-up. In the SC group, incidental prostate cancer was found in nine patients (18%).

None of the local recurrences in the PSC group was in the remnant prostatic urethra or prostate. However, in one patient recurrent carcinoma in situ in the prostatic urethra developed after a follow-up of 41 months. He was successfully treated with BCG.

Discussion

It is widely reported that PSC can preserve sexual function in up to 100% of patients.[3,4] In our study, information on erectile function was available in 55 of 63 patients. Five patients could not be evaluated because of early death and three were not sexually active after PSC. In almost 90% of these 55 evaluable patients erectile function could be maintained.

However, the oncological safety of PSC is controversial and intensively debated.[7,9] The oncological concerns against PSC are the presumed higher incidence of distant metastases, the risk of a local recurrence in the remaining prostate, and the risk of developing prostate cancer. The comparison between PSC and SC series is hampered by lack of randomized studies, different techniques and selection criteria.[10] In the absence of a randomized study we compared the outcomes of patients treated with a PSC or SC after matching for clinical and pathological criteria. However, this comparison is second best as compared to a randomized study. We acknowledge that our results have to be interpreted within the limitations of retrospective matching.

Stratified for these clinical and pathological factors we found no difference in survival. More importantly: no statistically significant difference was found in local recurrence rate (LRR) in the PSC group compared to the SC group (7.9% versus 16%, p=0.1). Although the median follow up in the PSC group (56 months) is significantly shorter than in the SC group (76 months), a median follow-up of more than four years in the PSC group is considered sufficient for the assessment of local recurrences, as most local recurrences come to light in the first two years after surgery.[11]

Local failure after cystoprostatectomy ranges from 7%-25%, depending on pathological stage.[12,13] In a population based study in the greater Amsterdam region comprising 18 hospitals, a LRR of 19% after cystectomy was found for all patients.[11] Local recurrence rates after prostate sparing procedures in other series range from 0 - 6.7%.[3,4,14] These lower rates can be explained by the selection of low risk patients, mostly non-muscle invasive bladder cancer. Only one report included also patients with locally advanced disease and positive lymph nodes, similar to our patient population, accounting for higher reported local and distant recurrence rates in this series. In the SC group, the distant recurrence rate is in the high region of the reported rates (33%, compared to 17-35% in the literature).[13,15] The rate of distant metastasis, 29% in the PSC group is within the reported range. Vallancien et al. found a distant recurrence rate of 34% in a patient group comparable to ours.[16] Other reports on prostate sparing procedures found an apparently higher distant recurrence rate than expected. Some authors suggested that TURP prior to PSC may be instrumental for metastatic spread of bladder cancer cells into the vessels of the prostate.[10] However preoperative TURP has not been our practice. Also direct tumour spill is suggested.[10] To diminish the risk of spill the ureters are clamped at an early phase during surgery and the bladder neck is closed immediately after dissection off the prostate.

Pettus et al. reported on the incidence of prostatic urothelial cancer (PUC) in cystoprostatectomy specimens. Risk factors for prostatic urothelial cancer were

tumour located at or distal to the trigone, and carcinoma in situ.[17] They found an incidence of PUC in cystoprostatectomy specimens of 33%-48%. While these data concern a population of unselected male bladder cancer patients treated with cystoprostatectomy, they are not applicable to patients in this series selected for PSC, where attention was focused on the identification of these risk factors. With success, exemplified by the fact that none of the local (urothelial cancer) recurrences in the PSC group occurred in the remaining prostatic urethra.

Two patients in the PSC group developed prostate cancer (3%). One was treated with external radiation therapy and died because of metastases of bladder cancer nine years after cystectomy. The other patient is being observed because of radiotherapy for concomitant colon cancer. He is still alive at 50 months of follow-up. This rate of detection in these selected patients is not at all uncommon. When reviewing the published series on PSC, consisting of more than 300 cases only 2 patients developed prostate cancer five years after surgery.[5,17] These rates are clearly different from the rates usually found in the literature. The reported incidence of incidental prostate cancer in unselected patients varies widely from 18%-46%.[13,18,19]

Incidental prostate cancer was found in 18% of the patients in the SC group. This percentage is relatively low as compared to the literature. However, the median age in the SC group was also relatively low as compared to other series[17,18] Standard removal of the prostate in this selected group of patients with bladder cancer is therefore not deemed necessary considering the low detection rate of prostate cancer. Moreover, with early detection due to a strict follow up all therapeutic modalities can be offered.

Most importantly no difference was seen in local and distant recurrence rate between both groups. In addition, outcomes of both procedures are comparable with contemporary cystoprostatectomy series.

Although patient numbers are small and patients undergoing a PSC are highly selected, we consider PSC for bladder cancer to be as safe as SC. Provided that patients eligible for PSC undergo a meticulous preoperative screening, focused on the presence of occult prostate cancer and risk factors for recurrence in the prostatic urethra. However, conclusions have to be interpreted within the limitations of retrospective matching.

Conclusions

Local or systemic recurrences were not diagnosed more frequently in the PSC group compared to the SC. After meticulous pre-operative screening the risk of both local recurrences in the remaining urothelium or clinically significant prostate cancer seems to be low. We consider this procedure oncologically safe and offer this to selected patients. However meticulous selection is the key to success and our results should further be corroborated by the experience of others.

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